TABLE I-continued

IN VITRO BONDING STRENGTH OF BIODEGRADABLE TISSUE ADHESIVES

Formula No.*	Bonding Strength, g/cm^2
4	196
Cyanoacrylate Adhesive	76

*Formula No.
1 5,000/THME,91/TDI,9/DABCO,0.05/CH_2Cl_2,40
2 5,000/PE,88/TDI,12/DABCO,0.1/CH_2Cl_2,40
3 10,000/THME,95/TDI,5/DABCO,0.03/CH_2Cl_2,40
4 10,000/THME,95/TDI,5/DABCO,0.1/CH_2Cl_2,40

Based on the in vitro bonding strength of the adhesive, animal studies were then undertaken using female Sprague-Dawley rats. Three parallel, longitudinal incisions were made through shaved skin over the dorsal anterior portion of the thorax of the rats. The left incision was closed with sutures, the middle incision was closed with the adhesive, and the right incision was closed with cyanoacrylate adhesive. The adhesives were formulated to adhere between 1 and 30 min. In some cases, animals reopened the wound sites of the experimental adhesive as well as the cyanoacrylate adhesive and the sutures by scratching at them. The experimental adhesives appeared to hold as well as the cyanoacrylate adhesive.

The following are some specific examples of adhesive formulations used in animal studies.

EXAMPLE 1

SINGLE COMPONENT SYSTEM

In this example, the single-component adhesive had the following composition, wt %.

Toluene diisocyanate, 63 wt %

Polyester composed of ethylene glycol-terminated 50:50 poly(DL-lactide)/ϵ-caprolactone, 37 wt %

Dibutyltin diacetate, 0.1 wt %

The adhesive was used to close incisions on the dorsal anterior portion of the thorax of rats. The incisions were closed with adhesive and held for 30 min. The incisions remained closed for three weeks, at which time the study was concluded. The in vitro tensile strength was 236 g/cm^2.

EXAMPLE 2

TWO COMPONENT SYSTEM

Examples of two-component adhesives are given in Table 1. Comparisons were made to cyanoacrylate adhesives. The formulations given in the footnotes follow the general scheme-theoretical molecular weight of prepolymer/initiator for poly(DL-lactide), wt % of polyester/type of diisocyanate, wt %/catalyst, wt %/solvent, wt % based on solids. Several observations can be made from the results of the studies. Although the first three adhesives were quite slow to cure, they all held successfully. In comparison, adhesives 4, 5 and 6 were faster to cure but in some cases failed to hold for the total testing period. Another factor contributing to the premature failure of some of the adhesives is the animals' scratching the incisions. This is evident from the fact that both the cyanoacrylate adhesive and sutures failed in many cases.

TABLE II

IN VIVO EFFICACY IN RATS OF TWO-COMPONENT ADHESIVES

Animal No.	Formula No.*	In vivo adhesion time, min	Day test formula opened	Day cyanoacrylate adhesive opened	Day sutures failed	Week killed
1	1	5			5	1
2	2	>5			2	1
3	2	>5			8	3
4	3	>5			3	3
5	3	>5	1	5		3
6	3	>5			3	1
7	4	1	2			1
8	4	1	4	4	4	3
9	4	1	4	1		2
10	5	2	8	4		1
11	5	2	1		8	3
12	5	2			8	2
13	6	6	4	4	9	2
14	6	6	1			1
15	6	3.5	8	4		3

*Formula No.
1 10,000/THME,87/MDI,13/DABCO,0.1/CH_2Cl_2,40.
2 10,000/THME,92/TDI,8/DABCO,0.1/CH_2Cl_2,40.
3 5,000/PE,81/TDI,19/DABCO,0.1/Ethyl acetate, 40.
4 5,000/THME,85/TDI,15/DABCO,1.5/Ethyl acetate, 40.
5 5,000/THME,85/TDI,15/DABCO,1.0/Ethyl acetate, 40.
6 5,000/THME,85/TDI,15/DABCO,0.75/Ethyl acetate, 40.

What is claimed is:

1. A method of producing an adhesive for use in joining soft living tissues comprising the steps of:

preparing a hydroxyl-terminated polyester by reacting a biodegradable monomer with a polyhydroxy polymerization initiator in the presence of a catalyst, wherein said monomer is selected from the group consisting of lactide, glycolide, ϵ-caprolactone and any combination thereof; and

preparing a diisocyanate-terminated prepolymer adhesive by reacting said hydroxyl-terminated polyester with excess aromatic diisocyanate.

2. The method of claim **1** wherein said initiator is selected from the group consisting of ethylene glycol, diethylene glycol, 1,1,1-tris (hydroxymethyl) ethane and pentaerythritol.

3. The method of claim **1** wherein said catalyst is selected from the group consisting of stannous octoate, zinc compounds, aromatic and aliphatic tertiary amines, 1,4-diazabicyclo [2,2,2]octane and dibutyltin diacetate.

4. The method of claim **1** wherein said aromatic diisocyanate is selected from the group consisting of toluene diisocyanate and methylene-bis-phenyl diisocyanate.

5. The method of claim **1** wherein said catalyst is present in an amount up to about 2.0 weight percent.

6. The method of claim **1** wherein said aromatic diisocyanate is added in amounts from about 8 to 76 percent and said hydroxyl-terminated polyester is added in amounts from about 24 to 92 weight percent.

7. The method of claim **1** further comprising the step of applying said prepolymer adhesive to soft living tissue whereupon said prepolymer adhesive is hydrolyzed to promote chain growth and cross linking to effect bonding to said tissue.

8. The method of claim **1** wherein said diisocyanate and said polyester are separated by a barrier within a package until just prior to use whereupon said barrier is removed to permit reaction therebetween.

9. The method of claim **1** wherein said aromatic diisocyanate and said polyester are mixed in an organic solvent in a ratio of solids to solvent of about 60:40.